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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,995	04/09/2001	Catherine A. McCall	AL-7	9579

26949 7590 10/23/2002

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EXAMINER
SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

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EXAMINER

ART UNIT	PAPER NUMBER
	16

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 8/12/02

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 24,25,28-30,34-40,43-47,49-51,53,54 is/are pending in the application.
Of the above, claim(s) 53,54 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 24,25,28-30,34-40,43-47,49-51 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☒ Claim(s) 24,25,28-30,34-40,43-47,49-51,53,54 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 9,10,12
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

Part III: Detailed Office Action

Notice: Effective June 18, 2000, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit **1647**.

Restriction Requirement:

Two restriction requirements were made in this application, see paper number 14.

In response to the first, Applicant's election of Invention I in Paper No. 15, filed 8/15/02, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

In response to the second, requiring applicants to elect among sequences, the Examiner spoke with applicant's attorney, Richard J. Stern, by telephone in August, 2002, requesting a clearer alignment of the various sequences. The attorney complied, supporting the arguments made in paper number 15 that examination of the claimed sequences would not present an undue burden. This argument is therefore, persuasive, and the second restriction requirement is **withdrawn.**

Claims 34 and 35 are rejoined with the elected group, as not presenting an undue search burden. Claims 53 and 54 are withdrawn from further consideration as being drawn to a non-elected invention. Claims 24, 25, 28-30, 34-40, 43-47 and 49-51 are under consideration.

Formal Matters:

The information disclosure statements submitted 8/23/01, 10/5/01 and 2/20/02. References by Kazuhiko et al. and Avery et al. have not been considered because they are merely sequences, the significance of which cannot be assessed in the absence of an alignment to the claimed sequences or alternatively a statement of relevance.

The title of the invention is not descriptive. A new title is required that is clearly indicative

of the invention to which the claims are directed.

Claims 24, 28, and 34 are objected to because of the following informalities: The claims overall are confusing for the repeated use of 'first, second, third', etc. to refer to proteins and nucleic acids. Applicants are advised to revise the claims to clarify such usages. Appropriate correction is required.

Applicants are advised that the UNITED STATES PATENT AND TRADEMARK OFFICE no longer regards recitations of "% identity" to be indefinite in the absence of a recited algorithm. Although not a grounds of objection, applicants may, if they wish, remove such recitations from the claims.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24, 25, 28-30, 34-40, 43-47 and 49-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 is indefinite for reciting "at least 40 contiguous nucleotide region" in part (a); it is not clear whether a single region of 40 contig. is intended, or rather 40 contiguous regions. The claim should be amended to recite *an* at least 40 contiguous nucleotide region to be remedial. The claim is further indefinite in part (b), as the claim requires 80% identity to *all* the recited sequence identifiers, whereas the specification would seem to indicate that a Markush group was actually intended. The inclusive term "and" should be deleted twice at line 4 and replaced with 'or', or alternatively after the word "to" at line 2, the phrase "a sequence selected from the group consisting of" should be inserted. Further, it is not clear whether "a fragment thereof" refers only to SEQ ID NO: 70, or to all the recited sequence identifiers.

Claim 28 is indefinite as it is not clear how a first protein can be selected from a group consisting of a second protein. The claim is further indefinite as part (a) (ii) appears to be circular (the second protein is at least 40 contig. amino acids of the first protein, which is identified as being selected from a group in which the second protein is a member) and cannot be interpreted.

The antecedent basis for "said protein" in claim 29 is not clear, as there are numerous proteins recited in claim 28, from which it depends.

Claim 34 is indefinite because it recites a "first" and "third" amino acid sequence, but there is no "second" amino acid sequence. The claim is further indefinite for using the inclusive "and a fragment thereof" in part (b); proper Markush language dictates either *or* in that phrase, or that the Markush group be preceded by the phrase "selected from the group consisting of..." Finally, it is not clear what limitation is imparted by the recitation that the DNAsis program is to be used for the comparison, in the absence of relevant parameters. See the suggestion above under "Formal Matters" to the effect that such language is superfluous to the claim.

Claim 36 is indefinite as it is not clear whether "a canine IL-13Rα2 protein domain" is intended to indicate that the entire IL-13Rα2 *is* a domain of the fusion protein, or alternatively that only one (of several) domains of IL-13Rα2 is present in the fusion protein. Claim 47 is similarly indefinite.

Claim 36 is also indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim says only that part (b) encodes a canine IL-13Rα2 protein domain, without any structural limitations. The specification as filed discloses two proteins, designated IL-13Rα1 and IL-13Rα2. Although the two presumably have different sequences and properties, the specification does not provide an adequate written description of the identifying features of the two, i.e. what would make a protein an IL-13Rα1 and not an IL-13Rα2, or vice versa. Thus, the metes and bounds of claim 36 cannot be determined, as the protein is referred to only by name, and as the specification fails to breath life and meaning into that name.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24,28, 29, 34, 35 and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids disclosed as SEQ ID NO: 54, 56, 57, 59, 60, 62-65, 67, 68 or 70 or fragments thereof (of specific lengths) or species which vary by codon degeneracy therefrom, as well as with proteins encoded thereby or fragments of said proteins that retain binding function or can be used to make antibodies reactive with said proteins, does not reasonably provide enablement for any nucleic acid comprising nucleic acids only 80% identical to a 50 nucleotide fragment of any of SEQ ID NOs: 54, 56, 57, 59, 60, 62-65, 67, 68 or 70. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claim 24 encompasses nucleic acids only 80% identical to a 50 nucleotide fragment of any of SEQ ID NOs: 54, 56, 57, 59, 60, 62-65, 67, 68 or 70. There is no functional limitation in the claim. Claim 28 encompasses nucleic acids which encode proteins only 70% identical to those disclosed, also without any functional limitation as regards the protein. Claim 34 encompasses proteins that comprise a region 70% identical to a 40 amino acid segment of said proteins, again with no functional recitation. Claim 29 adds the functional limitation that the protein encoded by the nucleic acid bind canine IL-13. Claim 34 encompasses proteins on 70% identical over a minimum of 40 amino acids of the disclosed protein sequences. Claim 35 contains additional limitations as to the encoding nucleic acid, to the effect that there must be 30 amino acids in common with the reference protein. There is no requirement that the 30 amino acids be at any particular portion of the protein. Claim 51 includes compositions comprising mimetopes of the disclosed proteins.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of

direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In this case, the nature of the invention is that applicants have discovered the canid IL-13 receptor alpha subunit. It is noted that applicants have apparently discovered two such subunit, and that it is the α2 subunit which is under consideration. The state of the art is that the human and murine forms of the protein were previously known, see U.S. Patent Number 5,710,023, cited by applicants. Although the relative skill in the art of recombinant DNA technology is high, little is known about the structure: function relationship for the particularly disclosed proteins, and the art of altering proteins is an uncertain one. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although there exist art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the

proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427). There is no guidance nor working examples of derivatives of the disclosed sequences. The lack of a working example is a factor to be considered, especially in a case involving an unpredictable art, as is the case here. As was found in Ex parte Hitzeman, 9 USPQ 2d 1821, a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope, as that scope encompasses proteins that bind IL-13 or nucleic acids encoding such. With respect to the scope of the claims as it reads upon species which do not have such binding activity, the specification has not taught any use for the protein other than binding IL-13, and thus fails how to use those species. To the extent that such species may be used to make antibodies, such only meet the written description requirement of 35 U.S.C. § 112, first paragraph to the extent that they have no novel epitopes. Any novel epitopes in such proteins have not been described, nor has the specification as filed taught how to use proteins comprising such.

With respect to mimetopes, as in claim 51, a mimetope is a protein that duplicates an

antigenic determinant, while having a distinct protein sequence. Thus, a mimetope is an antigenic 'functional equivalent'. The specification does not teach how to make such mimetopes, and enablement is not commensurate in scope with claims to any and all possible such mimetopes. The Examiner's position is supported by the decision in *Ex parte Maizel* (27 USPQ2d 1662 at 1665) that:

> Appellants have not chosen to claim the DNA by what it is but, rather, by what it does, i.e., encoding either a protein exhibiting certain characteristics, *or* a biologically functional equivalent thereof. Appellants' claims might be analogized to a single means claim of the type disparaged by the Court of Customs and Patent Appeals in *In re Hyatt,* 708F.2d 712, 218 USPQ 195 (Fed. Cir. 1983). The problem with the phrase "biologically functional equivalent thereof" is that it covers any conceivable means, i.e., cell or DNA, which achieves the stated biological result while the specification discloses, at most, only a specific DNA segment known to the inventor. Clearly the disclosure is not commensurate in scope with the claims."

In this case, applicants have disclosed a single protein that binds IL-13, and are claiming compositions comprising any and all proteins that share antigenicity with such. Clearly, enablement is not commensurate in scope with such a claim.

Claims 30 and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 51 includes compositions comprising mimetopes of the disclosed proteins. There is no written description of any mimetope of the disclosed protein in the specification, nor any description of any particular antigenic determinants to be mimicked by such.

Claim 30 has a negative limitation that the claimed nucleic acid molecule *not* hybridize to the nucleic acids represented by SEQ ID NO: 95-98, which are disclosed as the murine and human IL-13R binding chain (i.e. the murine and human orthologs of the disclosed canid IL-13Rα2) of U.S. Patent Number 5,710,023 respectively, and the reverse complement sequences of murine and human

IL-13R. This is a functional limitation. Given the sequence relatedness of the canid IL-13Rα2 disclosed in this specification to those orthologs (80.6% overall between human and dog, for example at the nucleic acid level), the Examiner is of the position that in trying to 'carve around' the art, applicants have drafted a claim that lacks written description, as there is no disclosure of any such molecules in the specification as originally filed, and due to the long regions of identity between the sequences, the Examiner is unable to envision even a single species within the metes and bounds of the claim.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, the claims do not meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 24, 28 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Collins et al., U.S. Patent Number 5,710,023.

Collins et al. disclose IL-13 receptor, nucleic acids encoding such, and pharmaceutical compositions comprising such (see abstract and col. 9). SEQ ID NO: 3 of Collins et al. comprises a fragment at least 80% identical to 50 nucleotides (e.g. at least 40/50 identity) of SEQ ID NO: 60, meeting the limitations of claim 24; see enclosed sequence alignment, for example at nucleotides 264-314 of SEQ ID NO: 60, which has a 47/50 match. The encoded protein is 70.5% identical to SEQ ID NO: 61, meeting the limitations of claim 28 and comprises regions of higher identity. Finally, the protein of Collins et al. would be considered a 'mimetope' of the protein of SEQ ID NO: 60, as the two share multiple epitopes, thus the pharmaceutical compositions of Collins et al. meet the limitations of claim 51.

Claim 24 is rejected under 35 U.S.C. 102(b) as being anticipated by any one of Guo et al., Genomics 42:141, Caput et al., J.B.C. 28:16921, Locus AI798934 or Locus AA298563.

As stated above, Claim 24 requires only a nucleic acid sequence that comprises a fragment at least 80% identical to 50 nucleotides of one or more of the recited sequences. All the cited references meet this limitation; see attached alignments.

Advisory Information:

No claim is allowed.

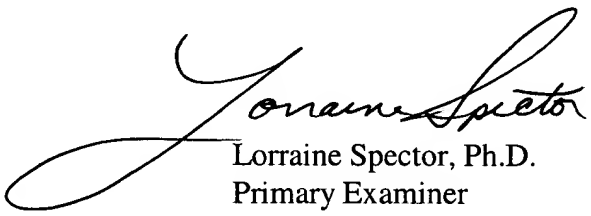
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.



Lorraine Spector, Ph.D.
Primary Examiner

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